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PPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
10/019,105	12/20/2001	Carlo Farina	P32331	7825
20462 75	90 01/14/2004		EXAMINER	
SMITHKLINE BEECHAM CORPORATION			LIU, HONG	
P. O. BOX 1539	PORATE INTELLECTUAL PROPERTY-US, UW2220 BOX 1539		ART UNIT	PAPER NUMBER
	SSIA, PA 19406-0939		1624	

Please find below and/or attached an Office communication concerning this application or proceeding.

		Application No.	Applicant(s)					
		10/019,105	FARINA ET AL.					
	Office Action Summary	Examiner	Art Unit					
		Hong Liu	1624					
Period fo	The MAILING DATE of this communication or Reply	appears on the cover sheet w	ith the correspondence address					
THE - Exte after - If the - If NO - Failu - Any earne	ORTENED STATUTORY PERIOD FOR RE MAILING DATE OF THIS COMMUNICATIO nsions of time may be available under the provisions of 37 CFF SIX (6) MONTHS from the mailing date of this communication e period for reply specified above is less than thirty (30) days, a poperiod for reply is specified above, the maximum statutory per re to reply within the set or extended period for reply will, by streply received by the Office later than three months after the med patent term adjustment. See 37 CFR 1.704(b).	N. R 1.136(a). In no event, however, may a reply within the statutory minimum of thin ind will apply and will expire SIX (6) MOI atute, cause the application to become A	reply be timely filed ty (30) days will be considered timely. NTHS from the mailing date of this communication. BANDONED (35 U.S.C. § 133).					
Status								
1)∐	Responsive to communication(s) filed on 1.							
- '-	,	his action is non-final.						
3)	Since this application is in condition for allo closed in accordance with the practice under							
Dispositi	on of Claims		_					
4)🖂	4)⊠ Claim(s) <u>1-8 and 16-19</u> is/are pending in the application.							
	4a) Of the above claim(s) is/are withdrawn from consideration.							
	5) Claim(s) is/are allowed.							
·	6)⊠ Claim(s) <u>1-8 and 16-19</u> is/are rejected.							
	Claim(s) is/are objected to. Claim(s) are subject to restriction an	d/or election requirement						
	on Papers	d/or election requirement.						
_	The specification is objected to by the Exam	iner						
	The drawing(s) filed on is/are: a) a		by the Examiner.					
	Applicant may not request that any objection to		·					
	Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).							
11)	The oath or declaration is objected to by the	Examiner. Note the attached	Office Action or form PTO-152.					
Priority u	ınder 35 U.S.C. §§ 119 and 120							
12)	Acknowledgment is made of a claim for fore	eign priority under 35 U.S.C.	§ 119(a)-(d) or (f).					
a) <sub>l</sub>	<ul><li>☐ All b) ☐ Some * c) ☐ None of:</li><li>1. ☐ Certified copies of the priority documents.</li></ul>	ents have been received.						
	<ul><li>2. Certified copies of the priority docum</li><li>3. Copies of the certified copies of the papplication from the International Bur</li></ul>	ents have been received in A riority documents have been eau (PCT Rule 17.2(a)).	received in this National Stage					
13) <u>∏</u> A si	See the attached detailed Office action for a scknowledgment is made of a claim for dome nce a specific reference was included in the 7 CFR 1.78.	estic priority under 35 U.S.C.	§ 119(e) (to a provisional application)					
. —	) $\square$ The translation of the foreign language		•					
	scknowledgment is made of a claim for dome eference was included in the first sentence o							
Attachmen	t(s)							
2) 🔲 Notic	e of References Cited (PTO-892) e of Draftsperson's Patent Drawing Review (PTO-948) nation Disclosure Statement(s) (PTO-1449) Paper No(s	5) Notice of I	Summary (PTO-413) Paper No(s)  nformal Patent Application (PTO-152)					

Art Unit: 1624

#### **DETAILED ACTION**

Claims 1-8 and 16-19 are pending in this application.

This action is in response to the applicants' amendment and reply filed on November 11, 2003.

#### **Response to Arguments**

Applicants' arguments and amendments filed on November 11, 2003 have been fully considered but they are not persuasive. Rejections of Claims 1-8 and 16-19 are maintained.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### Claim Rejections - 35 USC § 112

Claims 6-8 and 16-19 remain rejected under 35 U.S.C. 112, first paragraph for reasons already made of record and not withstanding applicants' traverse. These method claims remain non-enabled based solely on the over activity of osteoclasts relied on herein. Contrary to what applicants urge is enabled, there is no art-recognized evidence of clinical efficacy for the scope being claimed, and applicants have not provided an adequate traversal to refute the argument made by the examiner. As was previously mentioned in the last office action, Vasikaran's article indicated that inhibitors of osteoclast-mediated bone resorption are only useful in treating Paget's disease of bon, j-hypercalcaemia and osteolytic bone disease of malignancy, primary and secondary hyperparathyroidism and osteoprosis. Rather than providing evidence to support the argument that the instant compounds are indeed effective in treating all tumors and other diseases as claimed, applicants only generally stated that interpretation of the Vasikaran article is

Art Unit: 1624

"erroneous and contradictory if compared with the commonly accepted teaching derivable from the literature." Without providing specific evidence, the Examiner will have a difficult time to find the literature that is "erroneous and contradictory" to the Vasikaran article. The language in claim 8 that all the compounds represented by claim 1 can be used to treat tumors is not deemed to be scientifically sound as they are contrary to the current state of art in tumor and cancer treatment. In addition, attorney arguments cannot take the place of evidence on the record which applicants fail to supply (see MPEP 2145 I).

Therefore, in the absence of experimental evidence showing a nexus between osteoclasts antagonism and the effective treatment of all diseases associated with this specific mode of action, the method of treating, let alone preventing (porphylaxis), all diseases apparently contemplated and associated with these antagonists had not been enabled. Note the new utility guidelines stress that tests relied on must be recognized by those skilled in the art as reasonably predicative of in vivo efficacy in man the intended host. Note the remarks made in the recent decision, Genetech V. Novo Nordisk 42 USPQ2d 1001 for compliance with 35 U.S.C. 112, par. one., "This specification provides only a starting point, a direction, a direction for further research." while a different fact situation existed in that case the wording is appropriate herein. Of course the diseases urged supported by applicants are only exemplary and not all inclusive of the scope claimed in these claims.

Rejection #1) is maintained for reasons already made of record. There is no definition of the term in the specification.

Rejection #2) of the previous office action under 35 U.S.C. 112, second paragraph, is maintained for reasons already made of record. The claim language is not limited to one disease

Art Unit: 1624

and there is no clear indication of actual scope from a reading of the specification which describes a variety of disorders/conditions among a list that is nonlimiting. Nothing short of extensive testing would be needed to determine present scope, since the scope could alter over time with more reliable testing becoming available and more diseases being discovered to be affected by tyrosine kinase in ways not yet understood. Such uncertainty in scope does not comply with the second paragraph of 35 U.S.C. 112.

The rejection of the term "substituted and unsubstituted" is maintained for the reasons stated in the previous office. There is no disclosure in the specification what the substituents are.

### Claim Rejections - 35 USC § 102

All rejections under 35 U.S.C. § 102(a) are maintained. Contrary to applicants' arguments that none of the cited prior art teaches the compounds of formula (I) of claim 1, these references all anticipate the instant claims. For example, when R1 and R2 of the instant compound are hydrogen, Y is nitrogen and Z is carbon, R<sub>b</sub> is hydrogen, A is a substituted aryl, R<sub>s</sub> and R<sub>t</sub> are hydrogen, the compound is identical to compound 15 of Barraclough. When Y is carbon and Z is nitrogen and other variables remain the same, the instant compound is a tautomer of compound 4 of Barraclough.

## Claim Rejections - 35 USC § 103

Rejection under 35 U.S.C. § 103(a) is maintained for the same reason given in the above 102 rejection. There are compounds in the reference that anticipate the instant compounds. Since these compounds are species with the genus of the reference compounds, one of ordinary skill in

Art Unit: 1624

the art would be motivated to select similar compounds from the genus with the expectation that

the property of the compounds would remain the same.

Conclusion

1. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time

policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE

MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing

date of this final action.

Any inquiry concerning this communication should be directed to Examiner Hong Liu whose telephone number is (703) 306-5814. The examiner can normally be reached on Monday

through Friday from 8:30 AM to 6:00 PM.

If attempts to reach the examiner by the phone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached at (703) 308-4716. The fax phone number for the

organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding

should be directed to the receptionist whose telephone number is (703)/358-1235./

Mukundishah L. Rollmond / L. Supervisor Patent Examine Page 5

Art Unit 1624

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January 1, 2004